WHAT IS CLAIMED IS:

1. A biosensor comprising:

a) at least one mutated binding protein and at least one thiol group attached thereto; and

b) at least one sensor surface wherein said mutated binding protein is coupled through said thiol group to said surface;

wherein said at least one sensor surface provides a detectable signal resulting from a change in refractive index when said mutated binding protein binds to analyte.

2. The biosensor of claim 2 wherein said mutated binding protein is selected from glucose/galactose binding proteins.

3. The biosensor of claim 1 wherein said analyte is glucose or galactose.

4. The biosensor of claim 2 wherein said mutated glucose/galactose binding protein has one amino acid substitution.

5. The biosensor of claim 2 wherein said mutated glucose/galactose binding protein has at least two amino acid substitutions.

6. The biosensor of claim 3 wherein said mutated glucose binding protein includes one amino acid substitution selected from the group consisting of a cysteine at position 11, a cysteine at position 14, a cysteine at position 19, a cysteine at position 43, a cysteine at position 74, a cysteine at position 107, a cysteine at position 110, a cysteine at position 112, a cysteine at

position 113, a cysteine at position 137, a cysteine at position 149, a cysteine at position 213, a cysteine at position 216, a cysteine at position 238, a cysteine at position 287, a cysteine at position 292.

7. The biosensor of claim 4 wherein said mutated binding protein has at least one histidine tags.

8. The biosensor of claim 2 wherein said mutated glucose/galactose binding protein includes a cysteine present at position 213.

9. The biosensor of 8 wherein said mutated glucose binding protein further includes a histidine tag.

10. The biosensor of claim 2 wherein said mutated glucose binding protein includes a cysteine present at position 149 coupled to said sensor surface.

11. The biosensor of 10 wherein said mutated glucose binding protein further includes a histidine tag.

12. The biosensor of claim 5 wherein said mutated glucose binding protein includes at least two amino acid substitutions selected from the group consisting of: a cysteine at position 112 and a serine at position 238, a cysteine at position 149 and a serine at position 238, a cysteine at position 152 and a cysteine at position 182, a cysteine at position 152 and a serine at position 213, a cysteine at position 213 and a cysteine at position 238, a cysteine at position 149 and an arginine at position 213, a cysteine at position 149 and a serine at position 213 and a serine at

position 238, and a cysteine at position 149 and an arginine at position 213 and a serine at position 238 coupled to said sensor surface.

13. The biosensor of 12 wherein said mutated glucose binding protein further includes a histidine tag.

14. A method for analyte detection comprising:

a) providing at least one mutated binding protein and at least one thiol group attached thereto;

b) at least one sensor surface wherein said mutated binding protein is coupled through said thiol group to said surface;

c) exposing said mutated binding protein to biological solutions containing varying analyte concentrations;

d) detecting a detectable and reversible signal resulting from a change in refractive index;

wherein said detectable and reversible signal results from a change in refractive index upon binding corresponding to said varying analyte concentrations.

15. The method of claim 14 wherein said detecting is continuous, programmed, episodic, or combinations thereof.

16. The method of claim 14 wherein said at least one mutated binding protein is glucose/galactose binding protein.

17. The method of claim 14 wherein said detecting of detectable and reversible signals of varying analyte concentrations is *in vivo*.

18. The method of claim 17 wherein said analyte is glucose or galactose.

19. The method of claim 17 wherein said mutated glucose/galactose binding protein is selected from bacterial periplasmic binding proteins.

20. The method of claim 17 wherein said detecting of detectable and reversible signals from said reporter group of varying glucose concentrations is *in vivo*.

21. The method of claim 16 wherein said mutated glucose/galactose binding protein has one amino acid substitution.

22. The method of claim 17 wherein said mutated glucose/galactose binding protein has at least two amino acid substitutions.

23. The method of claim 21 wherein said one amino acid substitution is selected from the group consisting of a cysteine at position 11, a cysteine at position 14, a cysteine at position 19, a cysteine at position 43, a cysteine at position 74, a cysteine at position 107, a cysteine at position 110, a cysteine at position 112, a cysteine at position 113, a cysteine at position 137, a cysteine at

position 149, a cysteine at position 213, a cysteine at position 216, a cysteine at position 238, a cysteine at position 287, and a cysteine at position 292.

24. The method of claim 23 wherein said glucose/galactose binding protein has at least one histidine tag.

25. The method of claim 22 wherein said glucose/galactose binding protein has at least two amino acid substitutions selected from the group consisting of a cysteine at position 112 and a serine at position 238, a cysteine at position 149 and a serine at position 238, a cysteine at position 152 and a cysteine at position 182, a cysteine at position 152 and a serine at position 213, a cysteine at position 213 and a cysteine at position 238, a cysteine at position 149 and an arginine at position 213, a cysteine at position 149 and a serine at position 213 and a serine at position 238, and a cysteine at position 149 and an arginine at position 213 and a serine at position 238.

26. The method of claim 25 wherein said glucose/galactose binding protein has at least one histidine tag.

27. The method of claim 14, wherein said detectable and reversible signal is detected by surface plasmon resonance-based means.

28. The method of claim 14, wherein said detectable and reversible signal is detected by long period grating-based means.